

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application.

Listing of Claims:

1. (currently amended) An isolated nucleic acid encoding a protein comprising the amino acid sequence of SEQ ID NO: [[2 or]]8, ~~or a functional fragment thereof.~~
2. (currently amended) [[The]] An isolated nucleic acid encoding a polypeptide comprising a fragment of SEQ ID NO:8, the fragment being at least 10% of the length of SEQ ID NO:8, of claim 1, wherein the ~~protein-polypeptide~~ has [[a]] cytidine deaminase activity.
3. (currently amended) An isolated nucleic acid comprising the nucleotide sequence of nucleotides 80 to 676 of SEQ ID NO: [[1 or]]7, ~~or a fragment thereof.~~
4. (currently amended) An isolated nucleic acid comprising a nucleotide sequence ~~selected from the group consisting of:~~ complementary to
———~~(a) nucleotides 93 to 689 of SEQ ID NO:1; and~~
———~~(b) nucleotides 80 to 676 of SEQ ID NO:7.~~
5. (canceled)
6. (withdrawn) A substantially pure polypeptide comprising the amino acid sequence of SEQ ID NO:2 or 8 or a fragment thereof that (a) has a cytidine deaminase activity activity or (b) is immunogenic.
7. (withdrawn) A substantially pure polypeptide comprising substantially the same amino acid sequence as that of SEQ ID NO:2 or 8 and having a cytidine deaminase activity.
8. (withdrawn) A substantially pure polypeptide selected from the group consisting of:

(a) a mammalian polypeptide encoded by a nucleic acid that hybridizes under high stringency conditions to the sequence of SEQ ID NO:1, wherein the polypeptide has a cytidine deaminase activity; and

(b) a mammalian polypeptide encoded by a nucleic acid that hybridizes under high stringency conditions to the sequence of SEQ ID NO:7, wherein the polypeptide has a cytidine deaminase activity.

9. (original) An expression vector comprising the nucleic acid of claim 1.
10. (original) An expression vector comprising the nucleic acid of claim 2.
11. (original) An expression vector comprising the nucleic acid of claim 3.
12. (original) An expression vector comprising the nucleic acid of claim 4.
13. (canceled)
14. (original) A cultured host cell comprising the expression vector of claim 9.
15. (original) A cultured host cell comprising the expression vector of claim 10.
16. (original) A cultured host cell comprising the expression vector of claim 11.
17. (original) A cultured host cell comprising the expression vector of claim 12.
18. (canceled)
19. (withdrawn) An antibody or a reactive portion thereof to the polypeptide of claim 6.
20. (withdrawn) An antibody or a reactive portion thereof to the polypeptide of claim 7.
21. (withdrawn) An antibody or a portion thereof reactive to the polypeptide of claim 8.
22. (withdrawn) The antibody of claim 21, wherein the antibody is a monoclonal antibody.
23. (withdrawn) A pharmaceutical composition comprising the antibody or the portion thereof of claim 21 and a pharmaceutically acceptable carrier.
24. (withdrawn) A pharmaceutical composition comprising the antibody or the portion thereof of claim 22 and a pharmaceutically acceptable carrier.

25. (withdrawn) A cell producing a monoclonal antibody reactive to the polypeptide of claim 6.
26. (withdrawn) A cell producing a monoclonal antibody reactive to the polypeptide of claim 7.
27. (withdrawn) A cell producing a monoclonal antibody reactive to the polypeptide of claim 8.
28. (withdrawn) The cell of claim 25, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.
29. (withdrawn) The cell of claim 26, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.
30. (withdrawn) The cell of claim 27, wherein the cell is a hybridoma obtained by fusing, with a mammalian myeloma cell, a non-human mammalian B cell that produces a monoclonal antibody.
31. (withdrawn) The cell of claim 25, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.
32. (withdrawn) The cell of claim 26, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.
33. (withdrawn) The cell of claim 27, wherein the cell is a transgenic cell transformed by introducing, into the cell, either or both of a nucleic acid encoding a heavy chain of the monoclonal antibody and a nucleic acid encoding a light chain of the monoclonal antibody.
34. (withdrawn) An isolated nucleic acid comprising the nucleotide of (a) SEQ ID NO:9, (b) SEQ ID NO:10, or (c) SEQ ID NO:35.

35. (withdrawn) An isolated nucleic acid comprising the nucleotide selected from the group consisting of (a) SEQ ID NO:11, (b) SEQ ID NO:12, (c) SEQ ID NO:13, (d) SEQ ID NO:14, or (e) SEQ ID NO:15.

36. (currently amended) An isolated nucleic acid comprising the sequence ~~complementary to any one of:~~

- (a) SEQ ID NO:9, or
- ~~—— (b) SEQ ID NO: 10,~~
- ~~—— (c) SEQ ID NO: 11,~~
- ~~—— (d) SEQ ID NO: 12,~~
- ~~—— (e) SEQ ID NO: 13,~~
- ~~—— (f) SEQ ID NO: 14,~~
- ~~—— (g) SEQ ID NO: 15, or~~
- ~~—— (h) SEQ ID NO: 35,~~
- ~~—— (b) a sequence complementary to the full length of SEQ ID NO:9.~~

37. (currently amended) An isolated ~~oligonucleotide~~ nucleic acid comprising a continuous sequence complementary to a fragment of any one of over 20 bases that hybridizes to a probe consisting of:

- (a) nucleotides 1 to 1118 of SEQ ID NO: 9, in 0.9% NaCl at 75°C, or
- ~~—— (b) SEQ ID NO: 10,~~
- ~~—— (c) SEQ ID NO: 11,~~
- ~~—— (d) SEQ ID NO: 12,~~
- ~~—— (e) SEQ ID NO: 13,~~
- ~~—— (f) SEQ ID NO: 14,~~
- ~~—— (g) SEQ ID NO: 15, or~~

(b) a sequence complementary to nucleotides 1 to 1118 of SEQ ID NO: 9, in 0.9% NaCl at 75°C.

38. (withdrawn) The nucleic acid of claim 37, wherein the primer comprises a nucleotide

sequence of any one of:

- (a) SEQ ID NO:18,
- (b) SEQ ID NO:19,
- (c) SEQ ID NO:20,
- (d) SEQ ID NO:21,
- (e) SEQ ID NO:22,
- (f) SEQ ID NO:23,
- (g) SEQ ID NO:24,
- (h) SEQ ID NO:25,
- (i) SEQ ID NO:26,
- (j) SEQ ID NO:27,
- (k) SEQ ID NO:28,
- (l) SEQ ID NO:29,
- (m) SEQ ID NO:30,
- (n) SEQ ID NO:31,
- (o) SEQ ID NO:32,
- (p) SEQ ID NO:33, or
- (q) SEQ ID NO:34.

39. (withdrawn) A pair of isolated oligonucleotide primers selected from the group consisting of:

- (a) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:31 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:32,
- (b) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:20 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:22,
- (c) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:21 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:30,

(d) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:24 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:25,

(e) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:27,

(f) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

(g) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:23 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(h) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:27,

(i) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

(j) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:26 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(k) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:34 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:28,

(l) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:34 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29,

(m) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:33 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:29, or

(n) a nucleic acid comprising the nucleotide sequence of SEQ ID NO:18 and a nucleic acid comprising the nucleotide sequence of SEQ ID NO:19.

40. (withdrawn) A method for identifying a substance that regulates transcription of a gene encoding an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8 into mRNA, or production of the AID protein, the method comprising the steps of:

(a) culturing, separately in the presence and the absence of the substance, cells producing the AID protein, and

(b) (i) comparing the level of the AID protein produced by the cells cultured in the presence of the substance with the level of the AID protein produced by the cells cultured in the absence of the substance, or

(ii) comparing the level of the AID protein-encoding mRNA transcribed in the cells cultured in the presence of the substance with the level of the AID protein-encoding mRNA transcribed in the cells cultured in the absence of the substance.

41. (withdrawn) A method for identifying a substance that regulates transcription of a gene encoding an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8 into mRNA, or production of the AID protein, the method comprising the steps of:

(a) culturing, separately in the presence and the absence of the substance, cells producing the AID protein and a second protein other than the AID protein, wherein transcription of a gene encoding the second protein into mRNA is dependent in the cells on the degree of transcription of the gene encoding the AID protein into mRNA, and

(b) comparing the level of the second protein produced by the cells cultured in the presence of the substance with the level of the second protein produced by the cells cultured in the absence of the substance.

42. (withdrawn) The method of claim 40, wherein the cells are transgenic cells transformed with a gene encoding the AID protein.

43. (withdrawn) The method of claim 41, wherein the cells are transgenic cells transformed with a gene encoding the AID protein.

44. (withdrawn) The method of claim 41, wherein the cells are transgenic cells transformed with a gene encoding the AID protein and a gene encoding the second protein.

45. (withdrawn) The method of claim 41, wherein the second protein is a reporter protein.

46. (withdrawn) The method of claim 45, wherein comparison of the level of the second

protein is comparison of the level of a signal generated by the reporter protein.

47. (withdrawn) The method of claim 45, wherein the reporter protein is luciferase.

48. (withdrawn) A method for identifying a substance that inhibits an enzyme activity of an AID protein comprising the amino acid sequence of SEQ ID NO:2 or 8, the method comprising the step of:

(a) culturing, separately in the presence and the absence of the substance, mammal-derived B cells or tissues comprising the B cells, and comparing enzyme activities of the AID proteins in the B cells separately cultured, or

(b) (i) administering the substance separately to an AID gene knockout mouse whose endogenous AID gene is inactivated so that transcription of the endogenous AID gene into mRNA is inhibited, and to a normal mouse, and

(ii) comparing enzyme activities of the AID proteins in the B cells isolated from the respective mice.

49. (withdrawn) The method of claim 48, wherein the enzyme activity is a cytidine deaminase activity.

50. (new) An isolated nucleic acid encoding a polypeptide having a cytidine deaminase activity, wherein the nucleic acid:

(i) encodes a polypeptide fragment of SEQ ID NO: 8, the fragment comprising at least 70% of the length of the amino acid sequence of SEQ ID NO:8;

(ii) encodes a polypeptide that is at least 80% identical to the amino acid sequence of SEQ ID NO:8;

(iii) comprises a nucleotide sequence that is at least 80% identical to the coding sequence of SEQ ID NO:7; or

(iv) hybridizes to a probe the sequence of which consists of the coding sequence of SEQ ID NO:7, in 0.9% NaCl at 45°C.

51. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide comprising a fragment of SEQ ID NO:8, the fragment being at least 80% of the length of the amino acid sequence of SEQ ID NO:8.
52. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide comprising a fragment of SEQ ID NO:8, the fragment being at least 90% of the length of the amino acid sequence of SEQ ID NO:8.
53. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide that is at least 90% identical to SEQ ID NO:8.
54. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide that is at least 95% identical to SEQ ID NO:8.
55. (new) The nucleic acid of claim 50, wherein the nucleic acid comprises a nucleotide sequence that is at least 90% identical to the coding sequence of SEQ ID NO:7.
56. (new) The nucleic acid of claim 50, wherein the nucleic acid comprises a nucleotide sequence that is at least 95% identical to the coding sequence of SEQ ID NO:7.
57. (new) The nucleic acid of claim 50, wherein the nucleic acid hybridizes to a probe the sequence of which consists of the coding sequence of SEQ ID NO:7, in 0.9% NaCl at 55°C.
58. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide comprising the amino acid sequence of SEQ ID NO:8.
59. (new) The nucleic acid of claim 50, wherein the nucleic acid encodes a polypeptide comprising an amino acid sequence that is substantially the same as SEQ ID NO:8.
60. (new) An isolated nucleic acid comprising a continuous nucleotide sequence of over 20 bases of:
- (i) a nucleotide sequence that encodes a polypeptide fragment of SEQ ID NO:8, the fragment being at least 70% of the length of SEQ ID NO:8;

(ii) a nucleotide sequence that encodes a polypeptide that is at least 80% identical to the amino acid sequence of SEQ ID NO:8;

(iii) a nucleotide sequence that is at least 80% identical to the coding sequence of SEQ ID NO:7; or

(iv) a nucleotide sequence complementary to any one of (i) through (iii),
wherein the nucleic acid hybridizes to a nucleic acid the sequence of which consists of any one of (i) through (iv), in 0.9% NaCl at 75°C.

61. (new) An isolated nucleic acid that encodes a polypeptide consisting of the amino acid sequence of SEQ ID NO: 8.

62. (new) An isolated nucleic acid that is complementary to the nucleic acid of claim 61.

63. (new) An isolated nucleic acid comprising a sequence of over 20 continuous bases of nucleotides 80 to 676 of SEQ ID NO:7.

64. (new) An isolated nucleic acid comprising a nucleotide sequence complementary to over 20 continuous bases of nucleotides 80 to 676 of SEQ ID NO:7.

65. (new) An expression vector comprising a nucleic acid according to claim 50.

66. (new) A cultured host cell comprising an expression vector according to claim 65.

67. (new) An expression vector comprising a nucleic acid according to claim 51.

68. (new) A cultured host cell comprising an expression vector according to claim 67.

69. (new) An expression vector comprising a nucleic acid according to claim 52.

70. (new) A cultured host cell comprising an expression vector according to claim 69.

71. (new) An expression vector comprising a nucleic acid according to claim 53.

72. (new) A cultured host cell comprising an expression vector according to claim 71.

73. (new) An expression vector comprising a nucleic acid according to claim 54.

74. (new) A cultured host cell comprising an expression vector according to claim 73.
75. (new) An expression vector comprising a nucleic acid according to claim 55.
76. (new) A cultured host cell comprising an expression vector according to claim 75.
77. (new) An expression vector comprising a nucleic acid according to claim 56.
78. (new) A cultured host cell comprising an expression vector according to claim 77.
79. (new) An expression vector comprising a nucleic acid according to claim 57.
80. (new) A cultured host cell comprising an expression vector according to claim 79.
81. (new) An expression vector comprising a nucleic acid according to claim 58.
82. (new) A cultured host cell comprising an expression vector according to claim 81.
83. (new) An expression vector comprising a nucleic acid according to claim 59.
84. (new) A cultured host cell comprising an expression vector according to claim 83.
85. (new) An expression vector comprising a nucleic acid according to claim 60.
86. (new) A cultured host cell comprising an expression vector according to claim 85.
87. (new) An expression vector comprising a nucleic acid according to claim 61.
88. (new) A cultured host cell comprising an expression vector according to claim 87.
89. (new) An expression vector comprising a nucleic acid according to claim 62.
90. (new) A cultured host cell comprising an expression vector according to claim 89.
91. (new) An expression vector comprising a nucleic acid according to claim 63.
92. (new) A cultured host cell comprising an expression vector according to claim 91.
93. (new) An expression vector comprising a nucleic acid according to claim 64.
94. (new) A cultured host cell comprising an expression vector according to claim 93.

95. (new) A method of making a polypeptide that (i) is a fragment of SEQ ID NO:8, and comprises at least 70% of the length of the amino acid sequence of SEQ ID NO:8, or (ii) is at least 80% identical to the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 66.
96. (new) A method of making a polypeptide that comprises a fragment of SEQ ID NO:8, the fragment being at least 80% of the length of the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 68.
97. (new) A method of making a polypeptide that comprises a fragment of SEQ ID NO:8, the fragment being at least 90% of the length of the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 70.
98. (new) A method of making a polypeptide that is at least 90% identical to the full length of the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 72.
99. (new) A method of making a polypeptide that is at least 95% identical to the full length of the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 74.
99. (new) A method of making a polypeptide comprising the amino acid sequence of SEQ ID NO:8, the method comprising culturing a cell according to claim 82.
100. (new) A method of making a polypeptide comprising an amino acid sequence that is substantially the same as SEQ ID NO:8, the method comprising culturing a cell according to claim 84.
101. (new) A method of making a polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, the method comprising culturing a cell according to claim 88.